GRESHAM COLLEGE

15TH JANUARY 2020

PROSTATE & TESTICULAR CANCER

PROFESSOR CHRISTOPHER WHITTY

The last lecture in this series considered the major cancers which are almost exclusive to women. This lecture will consider the two major cancers of men; prostate cancer and testicular cancer. Prostate cancer is a very common disease of older men, most people with it will not die of it and many will be, for practical purposes, cured. It is also possible to live with prostate cancer as a chronic condition for many years. Testicular cancer is a much less common cancer of younger men which can often be cured with surgery. Testicular cancer has very good outcomes in the great majority of people who have it (>90%).

Prostate Cancer

Prostate cancer, in the sense of having cancerous cells, is extremely common as men age. In men who die of unrelated causes and subsequently undergo an autopsy, 50% to 60% of those in their 90s have evidence of prostate cancer of which they were often unaware and probably caused them no problems. In men under the age of 50 this is less than 0.5%, and it climbs every decade after that. This talk however is on prostate cancer significant enough to be diagnosed. But even these will often cause no symptoms, and many will require no or minimal treatment. Prostate cancer rates by age are shown in Figure 1 (CRUK data). In the UK around 47,000 cases a year are registered, making up around 26% of cancers in men. There is around a 16% lifetime risk for UK men born after 1960. Although, as this talk will demonstrate, the majority of prostate cancer is treated or controlled, it is still the second most frequent cause of cancer mortality in men because it is so common.

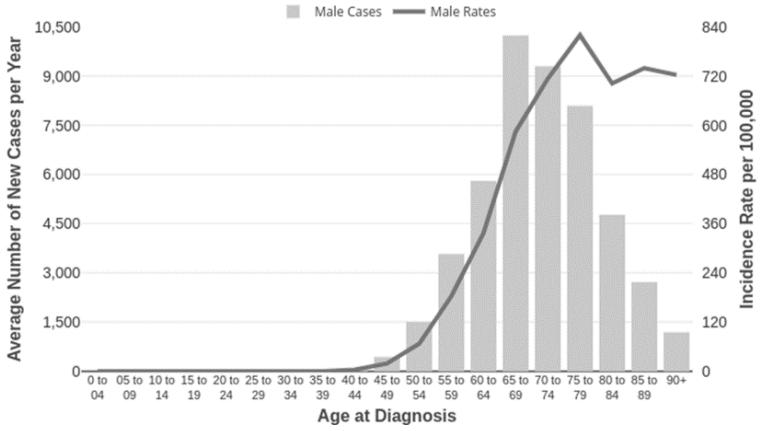

Figure 1

The prostate gland, which occurs only in men (or more accurately only in those born biologically male), is normally about the size of a chestnut. Its function is to produce seminal fluid and it has muscles to ejaculate. It also produces a hormone-like substance which mostly ensures sperm cells can move rapidly. It produces a number of enzymes including the important protein PSA, which makes semen thinner to allow sperm to swim in it. It also converts testosterone into its biologically active form. The prostate gets larger in older age, which is known as benign prostatic hyperplasia - this can cause urinary symptoms although it is not a cancer and sometimes needs surgical or medical treatment.

Symptoms that might be prostate cancer, but usually are *not* cancer include needing to pee frequently including at night, difficulty in starting to pee (hesitancy), weak flow and blood in urine or semen. With the exception of the blood, these are also the symptoms of benign prostatic enlargement. Many men who are diagnosed do not have symptoms. This may be through routine exam by a doctor or through a PSA test. PSA is raised in prostate cancer but other causes include benign prostatic hyperplasia, prostate infection, and physical pressure.

If men have raised PSA levels or other suspicions of cancer, they are likely to go onto imaging and possibly biopsy. Imaging may include an MRI scan or a transrectal ultrasound scan (TRUS). They may then have a biopsy under general or local anaesthetic. If a cancer is found it will be assessed for its stage, grade and type. The *stage* of the cancer is the size and degree of spread. The *grade* is the appearance of the cells; the more different from normal cells, the higher the grade. The *type* is the type of cell the cancer has arisen from. All of these have important implications for what is the correct treatment. More than 95% of prostate cancer is the adenocarcinoma type from mucus secreting glands. The remainder of types are all rare.

Most prostate cancer is diagnosed in Stages 1, 2 or 3. This means the cancer is within the prostate although it may just have broken through the prostate wall. Stage 4 cancer is if there is any spread whether local or to nodes or metastases. Most cancers have particular places they are likely to spread to, in the case of prostate cancer this tends to be *lymph nodes* in the abdomen and *bones,* in particular ribs, spine and pelvis.

Except for Stage 4, disease survival is very good in prostate cancer. Most men are diagnosed in Stages 1 to 3. Five-year cancer specific survival is almost 100% for Stages 1 and 2 and 95% for stage 3. Five-year survival is currently 49% for Stage 4 in the UK and 88% survival at a year. Survival rates are steadily rising (Figure 2). In the 1980s prostate cancer survival to 10 years was less than 30%; now it is over 80% and further improvements are likely. There have been some changes to the way cancer is diagnosed so some of this is artefact but much of this improvement is real. Treatment has also generally become less invasive, and with fewer side effects over time. An important development is the clear evidence that some men with prostate cancer need no treatment at all, just watchful waiting.

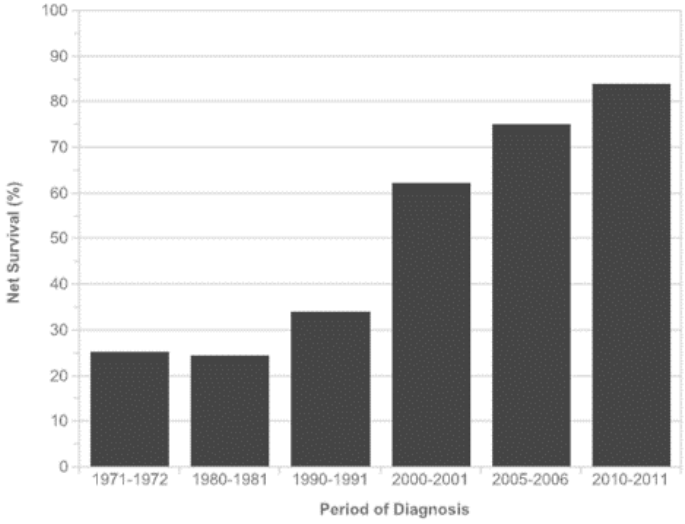

Figure 2

Given the survival rate is so much better if the cancer is identified before it gets to Stage 4, and this is a common disease, is reasonable to consider whether *screening* (as occurs in women for breast or cervical cancer) would be sensible. Several major trials have been conducted and using existing screening techniques, which is with the PSA blood test, the effect on mortality is for practical purposes zero. It does however lead to a significantly increased number of unnecessary biopsies and treatments. Therefore, with existing technology we are confident that screening is not worthwhile.

There is also clear trial evidence that in selected people with early prostate cancer, active monitoring with no intervention, surgery and radiotherapy have almost identical outcomes with virtually everybody surviving. For those who wish to, there are good online tools including some endorsed by the NHS to help understand the risks and benefits of treatment and discussions with your doctor.

For those who require treatment, the choices for early disease are between surgery and radiotherapy. Surgery is generally considered if the cancer is within the prostate, especially if it is fast-growing or in younger men. The usual surgical procedure is a radical prostatectomy which removes the prostate completely, sometimes with additional lymph nodes. It can be open, laparoscopic (keyhole) or robot assisted surgery. The main risks over the long term are urinary incontinence and erectile dysfunction in a minority.

Radiotherapy to treat cancer in the prostate can be delivered by external beam or locally. In either case radiotherapy damages and kills cancer cells but healthy cells usually recover. In addition to treating cancer confined to the prostate, it can be used to treat cancer that has spread or to alleviate symptoms, bone pain in particular. Radiotherapy is over a hundred years old. Modern radiotherapy is much more accurate meaning it damages less normal tissue and recent advances have included fewer and higher doses. External beam radiotherapy is when the radiotherapy beam passes through the patient with a maximum intensity of radiation only at the site of the tumour. An alternative way of radiotherapy to the prostate is brachytherapy, which means radiation emitting implants placed into the prostate. This may be combined with external beam radiotherapy. Long-term side-effects of radiotherapy can include incontinence, diarrhoea or erectile dysfunction but only a minority will suffer these. Short-term effects of radiotherapy include diarrhoea and localised hair loss and skin soreness. Many people tolerate radiotherapy very well.

For those who have metastases in the bones which are not under control, weakly-radioactive drugs can be injected into the vein which are taken up in the bone and kill cancer cells locally as an alternative to external beam radiotherapy.

Most prostate cancer cells are driven by testosterone, they are hormone dependent. Therefore, if testosterone is removed, the cancer cells shrink or die. Testosterone can be removed as a temporary adjunct to other treatment like radiotherapy to shrink the tumour, or as long-term suppression of advanced cancer or cancer that has recurred. Hormone treatment therapy options include switching off the production of testosterone in the testes by preventing the brain signalling production using luteinising hormone releasing hormone agonists; blocking testosterone reaching cancer cells using antiandrogen tablets; in a minority of cases removing testes (orchidectomy).

Chemotherapy is rarely used in prostate cancer, and usually any in an advanced cancer. The most commonly used drugs in the UK are taxanes, originally derived from the bark of the Pacific Yew.

A number of novel therapies are being explored, mainly in trials. These include high-intensity focal ultrasound to kill cancer cells by heating; cryotherapy to kill cancer cells by freezing; and proton beam therapy, a novel form of radiotherapy. Immunotherapy, which we discussed in the first lecture of this series, is being tried in advanced prostate cancer but so far proved less effective than some other cancers. Immunotherapy is however in its infancy and this may change over time. Arguably the most useful advance would be to be able to predict confidently which prostate cancers would remain indolent and require no treatment and which ones will become aggressive and require surgery or radiotherapy.

There are those who are considered to be of little or no modifiable risk for prostate cancer. Age is the major risk factor. Unlike most cancers this an inverse relationship with deprivation. Men of African and Afro-Caribbean heritage have a higher incidence of prostate cancer than white men, who in turn have a higher rate than people

with Asian heritage and there is both genetic and familial predisposition to prostate cancer. Obesity may increase the proportion of cancers that are aggressive, but not the risk of getting cancer.

Testicular Cancer

Testicular cancer is rare with around 2300 cases a year in the UK. It is a disease of young men, and rates of cure are very good with 98% surviving 10 years or more, up from around 70% in the 1970s. Peak incidence is in the 30s and is more common in white men and those in less deprived settings. The great majority of cases are diagnosed at an early stage by men finding a lump. Most swellings are not cancerous, but they should be checked. Diagnosis is by combination of ultrasound of the testes and blood markers for cancer. These can, with a high degree of accuracy, determine whether cancer is very likely and, in these cases, an orchidectomy of the affected testis is both diagnostic and usually curative.

After removal of a testes for cancer, most men can have a completely normal professional, romantic, and sexual life and also have children. An example is Bobby Moore, treated the testicular cancer in 1964, captained England to their (last) football World Cup victory in 1966, had children in 1965 and 68 and died in 1993 of an unrelated cancer.

The *stage* of cancer is determined by the degree of spread, which may be diagnosed either by CT scan or blood markers. In testicular cancer, the *type* of cancer is also very important for treatment. Cancers are divided into seminomas and non-seminomas. Seminomas are more sensitive to radiotherapy and chemotherapy and less prone to distant metastases, so non-seminomas require more aggressive treatment. Radiotherapy is mainly used for seminomas that have spread to the lymph glands of the abdomen. Chemotherapy is used for testicular cancer that has spread and is usually highly effective, and treatment courses are getting shorter.

Risk factors for testicular cancer are generally not majorly modifiable. Undescended testicles at puberty is a risk and correcting this reduces the risk. Family history of a father or brother having testicular cancer implies higher risk. Even in those with risk factors however testicular cancer remains very rare.

This talk has considered prostate cancer, a very common disease of older men, and testicular cancer an uncommon cancer of younger men. Diagnosed earl,y both of these have a very good prognosis, and even in late stage disease a substantial proportion of men will be alive and well many years later.

Further reading.

Cancer Research UK have an excellent site for both patients/family and medical professionals which cover prostate and testicular cancer. https://www.cancerresearchuk.org/about-cancer

The site for Prostate Cancer UK also has good information for people with, or who know someone with, the disease https://prostatecanceruk.org/

For medical professionals this recent review in *The Lancet* provides good additional information. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)61947-4/fulltext